

Villejuif, dec. 10, 1975

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RETURN TO HER

Dear Harold,

Thank you for your letters from dec. 1st, 75.

let me answer your questions.

I am now convinced that my earlier observations about sarc RNA not present in normal cells cannot be repeated. First your data indicate clearly that there is something there; second I have finally started hybridization experiments here and of course explored the presence of sarc RNA in normal cells: no question that I find results very similar to the ones you describe, my experiments being done in the same conditions that gave me the negative results nine month ago. In my hands, uninfected CEF 3° give 50% S1 resistance with cDNA_{sarc} (old probe), and ca 75% S1 resistance with cDNA_{sarc} (new probe) at a C_{ot} of 6×10^4 . With the old probe at the same conditions, I get a hybridization kinetic about 4 fold faster with QT6 RNA; do you get also such a difference?

The big question is "why were earlier experiments negative"? !?? I have no obvious explanation for that, specially since in one instance (embryos chf+) we had hybridization with cDNA_{S77}, this being to me a proof that the RNA was not notably degraded, and hybridization ^{had} occurred. Needless to say that I am awfully embarrassed with this turn of events. I understand now why I had positive results in my last experiments alone in SF (as I told you at the phone from Hershey), but doubted these results since they were only ~~one~~ ^{single} points few points at high C_{ot}, and not really C_{ot} curves. I agree with you that we should retract the Nature paper, exclude the RNA data, and I will also, on my side, explore the presence of sarc RNA in different cells and growth stages to try to clear the matter as quickly as possible. As a matter of fact, I think it would still be very interesting if there is a dose effect of sarc depending on growth stage or differentiation of the cells.

I was surprised that Mike asked me some old cDNA_{sarc} since I was pretty sure I had left quite a bit to Debbie; but from your letter I deduce that you did find it. We have to be carefull with it since, after what I sent to you, mine is essentially gone. But maybe it is not important anymore, since the new cDNA_{sarc} seems to

behave well. Enclosed is the detail of the preparation of the new sarc probe; its mainly in French but I am sure you will understand it. If problems, just tell me. Same with the RPL12 data..

Answering your question about the confluence of the CEF, QEF that I tested and found negative for sarc RNA, I did not write down specifically the state of the cells, but I am sure that they were very confluent terataries (since I wanted to get as much RNA out of them as possible). But, as you say, this would not explain the negative results observed with embryos. Talking about these RNAs, if there is any left, I did not bring it with me, so it should be in a rack in my freezer space there. But I doubt it.

I think I answered all your questions. Settling here was not an easy job (and still is'nt) and I am only now beginning to be able to do some experiments. Fortunately, I have a very nice and efficient technician working with me, and the main problems are not to have virus stocks and ready to use ^{32}P cDNA B77 ~~is~~ on hands, and to have to do without the good advices from you and Mike. Two days ago, I had the pleasure to receive a prize from the French Academy of Science (ca \$ 1400 : that was for sure very welcome) for my earlier work on protein sequencing and mass spectrometry (you see that things go pretty slowly in France!). Dominique and Chloé are doing fine, although I dont see them as much as I would like. Beside that, I really hope that I will be able to do some good work here, and not be too much distracted by the relaxed french way of life (I am mostly alone in the lab when I work at nights ~~or~~ or on Week ends). I am glad that you did find an alligator, and hope that you will find some sarc related sequences in its DNA.

Please say hello to all the people from the lab. I hope that Beegers basket ~~is~~ has not gone out of business since I left, and that I will have an opportunity to pay a visit to SF and all the friends that I miss, as soon as possible.

Best regards and merry Christmas to all of you

Dominiqne.